The bigger picture

The year is 1978. The city is London, England. On Waterloo Bridge, a man stands waiting patiently for a bus. Another man, dapperly dressed, passes him in the crowd, his closed umbrella swung like a marching band leader's baton – the picture of English propriety. No one notices when the second man's umbrella tip jabs into the leg of the first. But they *do* notice when the first man crumples to the ground in pain. As the man with the umbrella blithely walks on with his purposeful gait, someone asks the fallen man if he is all right; perhaps another attempts to raise him to his feet.

He doesn't move.

The man on the ground is dead of a heart attack: a blood clot has cut off the circulation to his heart, killing him.

At first glance, this looks like an event that happens every day: years of elevated cholesterol, high blood pressure, uncontrolled homocysteine or lipoprotein(a), a sedentary lifestyle, and empty Calories have taken their toll. But appearances can be deceiving.

The deceased is Bulgarian defector Gyorgi Markov. The man with the umbrella is an agent of East Germany's secret police. And there's a direct link between the umbrella jab -- so smoothly, so innocently executed -- and the blood clot that stopped a heart.

The umbrella tip had been coated with a protein, present in the castor oil plant (*Ricinus communis*), which binds to carbohydrates found on the surfaces of red blood cells. The protein entered into Markov's bloodstream and gummed up some of those cells; these formed a sort of artificial "clot," which blocked the flow of oxygen to the heart just as a natural blood clot would. A heart attack ensued.

It was a masterful assassination, using an almost perfect, unsuspected poison.

Would you believe that common foods you eat every day are loaded with similar molecules?

Lectins

The protein in the castor oil plant was one of a class of proteins called **lectins**. Very few lectins are as deadly as **Ricin**, the poison used to assassinate Markov[1] -- and, of course, you're unlikely to ever have any such toxin injected directly into your bloodstream. But the fact is that **many lectins found in common foods are still quite toxic when eaten** (see **Figure 2**). And **when foods containing these lectins are eaten, they may profoundly affect your health**.

Every cell in your body is covered in a variety of **receptors** -- loading docks for "payloads" delivered to the cells in the bloodstream. Many of these receptors are involved in the functioning of the body's immune system. These cell-surface markers branch out from the cell, presenting themselves like identification cards to the "bouncers" of the body's immune system. "Reading" these ID cards allows the body's immune system to tell friend from foe -- "self" from "non-self." The receptors that determine your main **blood type**, for instance -- **A, B, AB,** or **O** -- are cell-surface carbohydrates.

Lectins are proteins which bind to certain long-chain carbohydrate-based molecules. Many receptors are made up of just such molecules, so many lectins will bind to at least some cell types in the body. The effects of lectins in the body vary, however, because different lectins bind to different carbohydrate markers found on different cell types, and also because different lectins may bind to the *same* cell receptors, but with different tenacity. In any case, **nearly all cells from mammals have receptors which can be bound by at least some lectins**.

When lectins bind to cell surface markers, they impact the structure and functioning of those cells -- in some cases weakly, in others profoundly. Some of the hazards of dietary lectins are well-understood; others are at the moment largely speculative. But the potential impact of lectins on your health is too great to ignore -- especially since **lectins harmful to health are found in abundance in nearly all beans, legumes, and grains**.

Normal cooking, processing, and digestive processes do not guarantee the deactivation of lectins.

It's Alive!

Before going any further, it's probably best to dispel an oft-repeated myth. **Normal cooking, processing, and digestive processes do not guarantee the deactivation of lectins**. Some lectins have been reported to be highly resistant to normal digestive enzymes, such as **trypsin** and **pepsin**, and can tolerate acidity much more potent than that found in the stomach.[2] Some of the more potent lectins survive digestion almost in their entirety,[3] while at least 20% of some of the *most* easily digested lectins will survive the normal passage through the gut.[4]

For instance, one of the main lectins in wheat, **wheat germ agglutinin (WGA), is among the most commonly-consumed and potentially hazardous of dietary lectins** (as we will see). WGA is known to resist digestion and to be passed on through the GI into the feces, even after toasting,[5] which is not the usual practice.

Other **lectins found in wheat survive high-pressure cooking at 110°C for half an hour**.[6] A lectin found in kidney beans called **phytohemmaglutinin (PHA) maintains full lectin potency after four hours' cooking at temperatures**

The Lectin Epidemic?

commonly used in crock-pots (70°C), and even retains some activity after four hours' cooking at 85°C or three hours' cooking at 90°C.[7] Lectins in processed foods, such as **roasted peanuts and wheat-based breakfast cereals, have clearly-demonstrated lectin activity**.[8] The lectins in bananas actually have their binding powers *increased* by heating![9]

And, of course, **many lectin-rich foods, such as wheat germ, are commonly eaten raw** by health-conscious individuals ...

Figure 1. Binding Sites of Common Lectins[0,25]

Wheat (WGA)	Kidney, intestinal villii, myelin, breast.
Peanut (PNA)	Stomach (antral gland, Brunner's gland), kidney, breast, colon.
Kidney Bean (PHA)	Stomach (gastrin-secreting cells), digestive enzymes, myelin, pancreas, thyroid.

Lost Nutrition

The first health problem associated with lectins in the diet is **damage to the gastrointestinal (GI) tract**. Most lectins -- including common lectins found in grains and legumes -- bind to the carbohydrate markers on **microvilli**, the tiny, fingerlike projections which line the small intestine and which are used to absorb the nutrients in our food. This causes damage to the cellular "scaffolding" (**cytoskeleton**), a shortening of the microvilli, and a reduction in the amount of surface area available for nutrient absorption (see **Figure 4**).[3,10,11]

This damage to the microvilli directly inhibits the ability to take up nutrients, as does may lectins' tendency to literally *coat* the villi, interfering with absorption. Even at levels too low to cause visible damage to the intestines, some lectins can reduce absorption of lipids (and therefore of fat-soluble nutrients) and vitamin B_{12}.[12] Lectins can bind up, and inactivate, many digestive enzymes,[12] and interfere with the secretion of stomach acid.[13] The ability of some lectins to increase mucus production may also interfere with nutrient absorption.[14]

"Leaky Gut"

But lectin damage to the GI has implications far beyond a simple reduction in nutrient absorption – serious an issue as nutrient loss is, especially with today's processed, agrobusiness diets. **Lectins, including WGA and PHA, increase intestinal permeability ("leaky gut")**.[10,15,17] For those unfamiliar with this disorder, "leaky gut" is a condition in which the thin "gaskets" (**zonula occludens**) which bind the intestinal cells to one another are compromised. The zonula occludens is normally somewhat porous, allowing for the passage of very small, predigested molecules out of the GI and into the bloodstream. **In "leaky gut," these protective "gaskets" are either literally torn open, or become excessively porous**, allowing large molecules (like allergenic or otherwise unhealthy proteins) or even whole or partial pathogens (such as bacteria or yeast) to pass into the bloodstream and be carried throughout the body.

"Leaky gut" is a syndrome in and of itself, but is also a major contributor to the complications of disorders ranging from **Crohn's disease** and **inflammatory bowel disorder (IBD)** to **Celiac disease** and **AIDS**.[16] It can be caused, or exacerbated, by physical trauma, burns, and some drugs (such as **asprin** and **nonsteroidal anti-inflammatory drugs**).

In animal models, diets high in the wheat lectin WGA do not just damage the GI directly, but also inhibit the body's ability to defend itself from such damage using special stress-response molecules known as **heat-shock proteins (HSPs)**.[16a]

Giving experimental animals diets high enough in lectins to induce diarrhea has, in fact, been shown to cause *E. coli* and other GI bacteria to invade the lymph nodes in the membranes which join the intestines to the stomach.[18] And when the gut leaks, substances which are only a minor problem (or harmless, or even beneficial) in their proper environment can become serious health threats as they are transported to other parts of the body. Since lectins can create or worsen "leaky gut," their potential for harm should not be underestimated.

Pathogen Promoters

Lectins promote the overgrowth of some bacteria in the GI,[12] including ***E. coli*** and ***Streptococcus* bacteria.**[19,20] These changes happen within a day of beginning a high-lectin diet in experimental animals, and

Figure 2. Lectins with Known Oral Toxicity[26]

Peanut lectin (PNA)
Lentil lectin (LCL)
Winged bean (PTL or WBA)
Lima bean lectin (LBL)
Kidney bean lectin (PHA)
Wheat germ lectin (WGA)

while some of these bacteria begin to retreat again within 48 hours of withdrawing the high-lectin diet, others are more persistent. Lectins also aid the cause of other "nasties," such as **protozoan parasites**.[19]

A healthy colonic bacterial balance is important for overall health, and restoring this balance is the basis for supplementation with friendly bacteria like *Lactobacillus acidophilus*. However, evidence suggests that lectin-induced bacterial overgrowth may do more than upset the body's long-term probiotic balance. A recent animal study using **con A** (a lectin not found in the normal human diet) showed that feeding the animals the **lectin during *Salmonella* invasion caused the bacteria to more fully take over the gut, and worsened the severity of infection**.[21] We're most familiar with *Salmonella* as the cause of short-term food poisoning, but ongoing infection can lead to **paratyphoid fever**.

Beyond the GI

By now, you've got the message that lectins are bad news for the health of your digestive system. But many scientists now believe that the health problems caused by these molecules go well beyond the intestinal tract. As noted above, lectins promote "leaky gut," allowing substances which would normally be kept in the GI to be taken up into the bloodstream and carried away to distant parts of the body. The disturbing discovery was made in 1989 (and later confirmed) that **lectins**

themselves thus manage to penetrate the GI barrier and enter the bloodstream, ultimately binding to organs far removed from the digestive tract.[22-24] Especially disturbing was the fact that the lectins in question are from common foods -- such as wheat and peanuts. What are the implications of this discovery?

Autoimmune Disorders

Autoimmunity describes a situation in which the immune system mistakes the body's own tissues for foreign invaders and begins an ongoing attack on them, characterized by loss of function and chronic inflammation. Though most visible in such crippling diseases as **Type I diabetes, rheumatoid arthritis, lupus,** and the more common **thyroid disorders**, the fact is that the aging process causes a certain amount of low-level autoimmunity in everyone. There is now suggestive, but not conclusive, evidence that **the transport of lectins to the farther reaches of the body may cause, or accelerate, autoimmunity** in both visibly "healthy" people and victims of clear autoimmune disorders.

Wheat germ agglutinin (WGA) is among the most commonly-consumed and potentially hazardous of dietary lectins.

Lectins might play a role in autoimmunity in one of two main ways.[25,26]

False Alarm

One involves **changes to the immune markers** in the lectin-affected tissue. Most cells in the body only express markers which identify the cells as part the body's normal tissue. These self-markers are known as **class I HLA antigens**. But some cells in the body's immune system (such as **macrophages**) have a second type of marker (**class II HLA antigens**) which is used to help them sound the alarm that an invader has entered the body.

The alarm system works like this. A macrophage will bump into an enemy cell and consume it ("macrophage" literally means "major eater"). The macrophage then "burps up" the enemy cell's foreign markers, and places them side-by-side with the macrophage's own class II markers. Whenever other immune cells see a given marker side-by-side with a class II HLA antigen, they learn that the marker is the calling card of an invader. The body's immune system will then mount an immune assault on any cell bearing that marker.

As discussed above, lectins enter the bloodstream by penetrating a permeable, "leaky" intestinal tract, and are taken to other sites in the body, where they bind to the cells of a tissue with a complementary cell-surface carbohydrate (see **Figure 1**). But the binding of some lectins to cells isolated from the thyroids of patients with autoimmune thyroid disorders[27] or the pancreas[27a] causes them to express class II HLA antigens -- the special markers normally only seen on specialized immune cells. And, indeed, cells from thyroids of persons with autoimmune thyroid disorders do show extremely high rates of class II HLA antigens.[27b]

Unfortunately, these class II markers thus appear side-by-side with the cell's own, normal "self" markers – *exactly as would the markers of a pathogen consumed by a macrophage*. Researchers believe that their studies[27b,28] suggest that the body's immune system will react exactly as it would if those markers were presented next to class II markers on a macrophage. That is, the immune system will thereafter consider the body's normal immune markers as the calling card of the enemy, and launch an attack against them. An immune response to these cells would create **type I diabetes** in pancreatic cells or **Graves' disease or Hashimoto thyroiditis** in the thyroid. The same might apply in other cell types.

Mistaken Identification

A second, similar way that lectins might create or aggravate autoimmunity would be by **molecular mimicry**, a process in which the body's immune cells are presented with a foreign marker-molecule which is so similar to the normal marker of a body cell type that the immune system actually *confuses* the two. Having identified the foreign marker-molecule as an enemy's calling card, and confused it with the marker normally present on a given cell type, the immune system then attacks *both* the foreign material *and* the similar-looking body tissue. Long after the original invader is wiped out, the body still "sees" the signs of foreign material in the body's own cells, and continues its assault.[28]

A "self" marker commonly found in **rheumatoid arthritis** patients (technically, the "**Q(K/R)RAA"** amino acid sequence) exists which might be a cause of molecular mimicry, because it is very similar to markers found on *E. coli* and *L. lactis* bacteria, both of which are normally found in the GI. Fortunately, the body is not normally exposed to the foreign markers found on these bacteria, because the barrier presented by the intestinal wall prevents either the bacteria themselves, or their surface markers, from entering the bloodstream.

But what happens if these bacteria *do* manage to get across the GI wall, because of increased intestinal permeability – *such as the "leaky gut" known to be caused by high-lectin diets?* And what if a person is harboring an unusually high load of these two specific bacteria – *whose growth just happens to be stimulated by common dietary lectins?*[19] It's interesting, in this connection, to note that **conditions of heightened "leaky gut," such as Crohn's disease and celiac's disease, often accompany rheumatoid arthritis**[29-31] **and other autoimmune diseases**.[32]

The Lectin Epidemic?

The range of disorders in which lectins have been implicated is stunning. **Lectins**

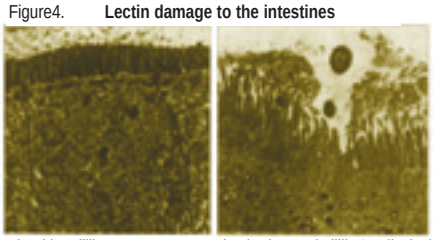
A Lectin Epidemic?

might be a factor in Berger's disease (IgA nephropathy),[33-35] **peptic ulcers,**[14,15,19,25] **arteriosclerosis,**[40] decline in T-cell immunity due to **shrinkage of the thymus,**[23] **and multiple sclerosis (MS).**[36-39] This article is hardly a comprehensive review, but merely attempts to draw your attention to the nature of the lectin problem, and the most active areas of research into the role of lectins in human disease. There are many other, more technical side-topics which we haven't even touched upon, such as the possible role of **viral infections** in making some people more susceptible to lectin-based damage.[39a] But the general picture message is probably clear: **lectins are a clear and present danger to your long-term health,** especially if you have certain existing health problems.

Eat Right: 4-get Your Type

If you're now scared of lectins -- well, you're not alone. Millions have become concerned about potentially negative impact of lectins on health through the bestselling book *Eat Right 4 Your Type.*[47] While the book has served as a valuable wakeup call on the lectin issue, its contents are a bemusing mixture of science and superstition, established fact and long-disproven theories. In particular, it's long been known that **the A and B blood types are found in other primates**, including gorillas, orangutans, gibbons, chimpanzees, and macaque monkeys,[41-45] **and have existed for at least three million years**[46] -- and thus clearly cannot have evolved in response to changes in the human diet after the agricultural revolution beginning in the Near East in approximately 8 000 BCE.

Figure4. **Lectin damage to the intestines**



healthy villii — lectin damged villii Credit: (51)

The fact is that, while the various blood groups *are* more sensitive to some lectins than to others, and thus the "lectin invasion" might have some effects unique to the blood types, the tissues which are affected most clearly and most harmfully by common dietary lectins are not made more or less susceptible to lectins based on blood type. So **avoiding grain and legume lectins makes as much sense for a type A or B as a type O**.

Why, then, do so many people do so well on the program prescribed for their blood type? There are a number of reasons, but probably the most important one is the simple fact that **the diets prescribed will be an improvement on the Standard American Diet (SAD)** for almost anyone.

In particular, the single most common blood type is O. The Type O diet is rich in high-nutrition, low-lectin, sugar-stabilizing vegetables, and lower in nutrient-poor, lectin-filled, blood-sugar spiking grains -- smart advice for anyone. Even the vegetarian Type A diet is much lower in grains than the "Food Pyramids" advocated by Canadian and US health authorities. Type Os following D'Adamo's plan will also find themselves consuming better-quality protein, and in higher amounts; many women who are health-conscious have been mistakenly following diets far too low in quality protein, so the change to the Type O plan will represent a real nutritional advance. And none of the diets leave much room for the refined carbohydrates, saturated fat, and other garbage foods common to the typical North American table.

Get the Lectin Out!

Despite all of the negative impacts of many dietary lectins, some lectins are actually a healthy choice for some people, some of the time. For instance, because they appear to prevent the proliferation of a type of skin cell (**keratinocytes**), lectins present in the common mushroom (*Agaricus bisporus*) might be of benefit in psoriasis,[48] while other mushroom lectins apparently inhibit the growth of cancer cells.[49] The concern is ultimately not with lectins per se, but with a few "bad" lectins. Unfortunately, while the most toxic lectins have been screened out of the normal human diet by generations of trial and error (no one serves castor oil seeds as a bar snack!), there are still significant health hazards posed by lectins commonly found in dietary staples: beans, legumes, and grains. So what can be done to root out the common vandals hiding in our food?

One vital step in reducing "bad" lectin exposure is to **always be sure to thoroughly cook dry beans**. Full-blown, acute food poisoning occurs in many people every year from undercooked beans. According to the US FDA, which does not acknowledge a role for lectins in *chronic* disease (all emphasis ours), "The syndrome is usually caused by the ingestion of raw, soaked kidney beans, either alone or in salads or casseroles. *As few as four or five raw beans can trigger symptoms*. Several outbreaks have been associated with 'slow cookers' or crock pots, or in casseroles which had not reached a high enough internal temperature to destroy the glycoprotein lectin. It has been shown that heating to 80°C may *potentiate the toxicity five-fold*, so that *these beans are more toxic than if eaten raw*. In studies of casseroles cooked in slow cookers, internal temperatures often did not exceed 75°C."[50] Presoaking beans before cooking also significantly reduces the lectin load of the final dish.

Another important step is to consider **reducing your intake of those lectin-rich foods which are difficult to neutralize** because they are either normally eaten almost raw (**peanuts** and **wheat germ**) or are never cooked adequately to truly neutralize lectin activity (**grains, and especially wheat**).

This doesn't mean you have to literally go "back to the stone age" with your diet, eliminating the agriculture-based foods that contain the lectins which are the biggest offenders. But we've made these foods health staples, and we have to learn to understand -- and manage -- their unique risks.

A Lectin Epidemic?
References

0. Freed DL. Dietary lectins and disease. In Brostoff and Callacombe (eds), Food Allergy and Intolerance. 1987; Toronto: Balliere Tindall, 375-400. The author is especially indebted to this review for identifying key issues and references.

1. Knight B. Ricin s a potent homicidal poison. BMJ. 1979 Feb 3;1(6159):350-1.

2. Nachbar MS, Oppenheim JD, Thomas JO. Lectins in the U.S. Diet. Isolation and characterization of a lectin from the tomato (Lycopersicon esculentum). J Biol Chem. 1980 Mar 10;255(5):2056-61.

3. Pusztai A, King TP, Clarke EM. Recent advances in the study of the nutritional toxicity of kidney bean (Phaseolus vulgaris) lectins in rats. Toxicon. 1982;20(1):195-7.

4. Pusztai A. Dietary lectins are metabolic signals for the gut and modulate immune and hormone functions. Eur J Clin Nutr. 1993 Oct;47(10):691-9.

5. Brady PG, Vannier AM, Banwell JG. Identification of the dietary lectin, wheat germ agglutinin, in human intestinal contents. Gastroenterology. 1978 Aug;75(2):236-9.

6. Concon JM, Newburg DS, Eades SN. Lectins in wheat gluten proteins. J Agric Food Chem. 1983 Sep-Oct;31(5):939-41.

7. Grant G, More LJ, McKenzie NH, Pusztai A. The effect of heating on the haemagglutinating activity and nutritional properties of bean (Phaseolus vulgaris) seeds. J Sci Food Agric. 1982 Dec;33(12):1324-6.

8. Nachbar MS, Oppenheim JD. Lectins in the United States diet: a survey of lectins in commonly consumed foods and a review of the literature. Am J Clin Nutr. 1980 Nov;33(11):2338-45.

9. Gibbons RJ, Dankers I. Lectin-like constituents of foods which react with components of serum, saliva, and Streptococcus mutans. Appl Environ Microbiol. 1981 Apr;41(4):880-8.

10. Sjolander A, Magnusson KE, Latkovic S. Morphological changes of rat small intestine after short-time exposure to concanavalin A or wheat germ agglutinin. Cell Struct Funct. 1986 Sep;11(3):285-93.

11. Lorenzsonn V, Olsen WA. In vivo responses of rat intestinal epithelium to intraluminal dietary lectins. Gastroenterology. 1982 May;82(5 Pt 1):838-48.
12. Banwell JG, Boldt DH, Meyers J, Weber FL Jr. Phytohemagglutinin derived from red kidney bean (Phaseolus vulgaris): a cause for intestinal malabsorption associated with bacterial overgrowth in the rat. Gastroenterology. 1983 Mar;84(3):506-15.

13. Kordas K, Burghardt B, Kisfalvi K, Bardocz S, Pusztai A, Varga G. Diverse effects of phytohaemagglutinin on gastrointestinal secretions in rats. J Physiol Paris. 2000 Jan-Feb;94(1):31-6.

14. Freed DL, Buckley CH. Mucotractive effect of lectin. Lancet. 1978 Mar 18;1(8064):585-6.

15. Greer F, Pusztai A. Toxicity of kidney bean (Phaseolus vulgaris) in rats: changes in intestinal permeability. Digestion. 1985;32(1):42-6.

16. Hollander D. Intestinal permeability, leaky gut, and intestinal disorders. Curr Gastroenterol Rep. 1999 Oct;1(5):410-6.

16a. Ovelgonne JH, Koninkx JF, Pusztai A, Bardocz S, Kok W, Ewen SW, Hendriks HG, van Dijk JE. Decreased levels of heat shock proteins in gut epithelial cells after exposure to plant lectins. Gut. 2000 May;46(5):679-87.

17. Nishihata T, Burton PR, Caldwell LJ. Induction of microvillous fusion and pinching-off by concanavalin A. Biochem Biophys Res Commun. 1986 Oct 30;140(2):766-72.

18. Shoda R, Mahalanabis D, Wahed MA, Albert MJ. Bacterial translocation in the rat model of lectin induced diarrhoea. Gut. 1995 Mar;36(3):379-81.

19. Banwell JG, Howard R, Kabir I, Costerton JW. Bacterial overgrowth by indigenous microflora in the phytohemagglutinin-fed rat. Can J Microbiol. 1988 Aug;34(8):1009-13.

20. Ceri H, Falkenberg-Anderson K, Fang RX, Costerton JW, Howard B, Banwell JG. Bacteria-lectin interactions in phytohemagglutinin-induced bacterial overgrowth of the small intestine. Can J Microbiol. 1988 Aug;34(8):1003-8.

21. Naughton PJ, Grant G, Bardocz S, Pusztai A. Modulation of Salmonella infection by the lectins of Canavalia ensiformis (Con A) and Galanthus nivalis (GNA) in a rat model in vivo. J Appl Microbiol. 2000 Apr;88(4):720-7.

22. Pusztai A, Greer F, Grant G. Specific uptake of dietary lectins into the systemic circulation of rats. Biochem Soc Trans. 1989 Jun; 17(3):481-2.

23. Pusztai A, Ewen SW, Grant G, Brown DS, Stewart JC, Peumans WJ, Van Damme EJ, Bardocz S. Antinutritive effects of wheat-germ agglutinin and other N-acetylglucosamine-specific lectins. Br J Nutr. 1993 Jul;70(1):313-21.

24. Wang Q, Yu LG, Campbell BJ, Milton JD, Rhodes JM. Identification of intact peanut lectin in peripheral venous blood. Lancet. 1998 Dec 5;352(9143):1831-2.

25. Freed DL. Do dietary lectins cause disease? BMJ. 1999 Apr 17;318(7190):1023-4.

26. Cordain L, Toohey L, Smith MJ, Hickey MS. Modulation of immune function by dietary lectins in rheumatoid arthritis. Br J Nutr. 2000 Mar;83(3):207-17.

27. Weetman AP, Volkman DJ, Burman KD, Gerrard TL, Fauci AS. The in vitro regulation of human thyrocyte HLA-DR antigen expression. J Clin Endocrinol Metab. 1985 Nov;61(5):817-24.

27a. Pujol-Borrell R, Todd I, Doshi M, Gray D, Feldmann M, Bottazzo GF. Differential expression and regulation of MHC products in the endocrine and exocrine cells of the human pancreas. Clin Exp Immunol. 1986 Jul;65(1):128-39.

27b. Zantut-Wittmann DE, Boechat LH, Pinto GA, da Silva Trevisan MA, Vassallo J. Autoimmune and non-autoimmune thyroid diseases have different patterns of cellular HLA class II expression. Sao Paulo Med J. 1999 Jul 1;117(4):161-4.

28. Faure GC, Bensoussan-Lejzerowicz D, Bene MC, Aubert V, Leclere J. Coexpression of CD40 and class II antigen HLA-DR in Graves' disease thyroid epithelial cells. Clin Immunol Immunopathol. 1997 Aug;84(2):212-5.

29. Hazenberg MP, Klasen IS, Kool J, Ruseler-van Embden JG, Severijnen AJ. Are intestinal bacteria involved in the etiology of rheumatoid arthritis? APMIS. 1992 Jan;100(1):1-9.

30. Lepore L, Martelossi S, Pennesi M, Falcini F, Ermini ML, Ferrari R, Perticarari S, Presani G, Lucchesi A, Lapini M, Ventura A. Prevalence of celiac disease in patients with juvenile chronic arthritis. J Pediatr. 1996 Aug;129(2):311-3.

31. Collin P, Maki M. Associated disorders in coeliac disease: clinical aspects. Scand J Gastroenterol. 1994 Sep;29(9):769-75.

32. Kaukinen K, Collin P, Mykkanen AH, Partanen J, Maki M, Salmi J. Celiac disease and autoimmune endocrinologic disorders. Dig Dis Sci. 1999 Jul;44(7):1428-33.

33. Holthofer H. Lectin binding sites in kidney. A comparative study of 14 animal species. J Histochem Cytochem. 1983 Apr;31(4):531-7.

34. Holthofer H, Virtanen I. Glycosylation of developing human glomeruli: lectin binding sites during cell induction and maturation. J Histochem Cytochem. 1987 Jan;35(1):33-7.

35. Coppo R, Amore A, Roccatello D. Dietary antigens and primary immunoglobulin A nephropathy. J Am Soc Nephrol. 1992 Apr;2(10 Suppl):S173-80.

36. Quarles RH, McIntyre LJ, Pasnak CF. Lectin-binding proteins in central-nervous-system myelin. Binding of glycoproteins in purified myelin to immobilized lectins.

37. Biochem J. 1979 Nov 1;183(2):213-21. 37. Hukkanen V. Lectin-reactive components in white matter membranes from normal and multiple sclerosis brains. J Neurochem. 1982 Jun;38(6):1537-41. 3
8. Yacyshyn B, Meddings J, Sadowski D, Bowen-Yacyshyn MB. Multiple sclerosis patients have peripheral blood CD45RO+ B cells and increased intestinal permeability. Dig Dis Sci. 1996 Dec;41(12):2493-8.

39. McIntyre LJ, Quarles RH, Brady RO. Lectin-binding proteins in central-nervous-system myelin. Detection of glycoproteins of purified myelin on polyacrylamide gels by [3h]concanavalin A binding. Biochem J. 1979 Nov 1;183(2):205-12.

39a. Klein PJ, Bulla M, Newman RA, Muller P, Uhlenbruck G, Schaefer HE, Kruger G, Fisher R. Thomsen-Friedenreich antigen in haemolytic-uraemic syndrome. Lancet. 1977 Nov 12;2(8046):1024-5.

40. Kritchevsky D, Tepper SA, Klurfeld DM. Lectin may contribute to the atherogenicity of peanut oil. Lipids. 1998 Aug;33(8):821-3.

41. Lu YQ, Liu JF, Socha WW, Nagel RL, Blumenfeld OO. Polymorphism of glycophorins in nonhuman primate erythrocytes. Biochem Genet. 1987 Aug;25(7-8):477-91.

42. Socha, W.W. et al. (1976). Blood groups of bonnet macaques (Macaca radiata), with a brief introduction to seroprimatology. Am J Phys Anthrop 45:485-491.

43. Socha WW, Blancher A, Moor-Jankowski J. Red cell polymorphisms in nonhuman primates: a review. J Med Primatol. 1995 Dec;24(4):282-305.

44. Moor-Jankowski J. Blood groups of primates: historical perspective and synopsis. J Med Primatol. 1993 Jan;22(1):1-2.

45. Landsteiner K, Miller CP. Serological observations on the relationship of the bloods of man and the anthropoid apes. Science. 1925 May 8; 61(1584):492-3.

46. O'hUigin C, Sato A, Klein J. Evidence for convergent evolution of A and B blood group antigens in primates. Hum Genet. 1997 Dec;101(2):141-8.

47. D'Adamo PJ, Whitney C. Eat Right 4 Your Type. 1996. New York, NY: GP Putnam's Sons.

48. Parslew R, Jones KT, Rhodes JM, Sharpe GR. The antiproliferative effect of lectin from the edible mushroom (Agaricus bisporus) on human keratinocytes: preliminary studies on its use in psoriasis. Br J Dermatol. 1999 Jan;140(1):56-60.

49. Yu LG, Fernig DG, White MR, Spiller DG, Appleton P, Evans RC, Grierson I, Smith JA, Davies H, Gerasimenko OV, Petersen OH, Milton JD, Rhodes JM. Edible mushroom (Agaricus bisporus) lectin, which reversibly inhibits epithelial cell proliferation, blocks nuclear localization sequence-dependent nuclear protein import. J Biol Chem. 1999 Feb 19;274(8):4890-9.

50. http://vm.cfsan.fda.gov/~mow/chap43.html

51. Liener IE, Sharon N, Goldstein IJ. The Lectins: Properties, Functions, and Applications in Biology and Medicine. Toronto: Academic Press Inc., 1986.